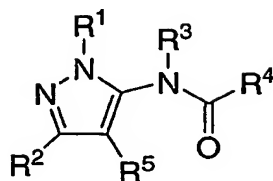


WHAT IS CLAIMED IS:

1. A compound of the formula I:



I

wherein:

R¹ is selected from the group consisting of:

- (1) hydrogen,
- (2) C₁-6alkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl,
- (3) C₃-7cycloalkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl, and
- (4) phenyl, which is unsubstituted or substituted with one or more substituents independently selected from:
 - (a) -C₁-6alkyl,
 - (b) -O-C₁-6alkyl,
 - (c) halo,
 - (d) hydroxy,
 - (e) trifluoromethyl,
 - (f) -OCF₃,
 - (g) -CO₂R⁹,

wherein R⁹ is independently selected from:

- (i) hydrogen,
- (ii) -C₁-6alkyl, which is unsubstituted or substituted with 1-6 fluoro,
- (iii) benzyl, and
- (iv) phenyl,
- (h) -NR¹⁰R¹¹,

wherein R¹⁰ and R¹¹ are independently selected from:

- (i) hydrogen,
- (ii) -C₁-6alkyl, which is unsubstituted or substituted with 1-6 fluoro,
- (iii) -C₅-6cycloalkyl,

- (iv) benzyl,
 (v) phenyl,
 (vi) -S(O)₂-C₁₋₆alkyl,
 (vii) -S(O)₂-benzyl, and
 (viii) -S(O)₂-phenyl,
 (i) -CONR¹⁰R¹¹, and
 (j) -NO₂;
- (5) heterocycle, wherein heterocycle is selected from:
 benzoimidazolyl, benzimidazolonyl, benzofuranyl, benzofurazanyl,
 benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl,
 carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolaziny, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthpyridinyl, oxadiazolyl, oxazolyl, oxazoline, isoxazoline, oxetanyl, pyranyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, tetrahydropyranyl, tetrazolyl, tetrazolopyridyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidiny, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyridin-2-onyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzoimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidiny, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl, and N-oxides thereof, which is unsubstituted or substituted with one or more substituents independently selected from:
 (a) -C₁₋₆alkyl,
 (b) -O-C₁₋₆alkyl,
 (c) halo,
 (d) hydroxy,
 (e) phenyl,
 (f) trifluoromethyl,
 (g) -OCF₃,
 (h) -CO₂R⁹,

- (i) -NR¹⁰R¹¹, and
- (j) -CONR¹⁰R¹¹;

R² and R⁵ are independently selected from the group consisting of:

- 5 (1) hydrogen,
- (2) C₁₋₆alkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl,
- (3) C₃₋₇cycloalkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl, and
- 10 (4) phenyl, which is unsubstituted or substituted with one or more substituents independently selected from:
 - (a) -C₁₋₆alkyl, which is unsubstituted or substituted with -NR¹⁰R¹¹,
 - (b) -O-C₁₋₆alkyl,
 - (c) halo,
 - 15 (d) hydroxy,
 - (e) trifluoromethyl,
 - (f) -OCF₃;
 - (g) -CO₂R⁹,
 - (h) -NR¹⁰R¹¹,
 - 20 (i) -C(O)NR¹⁰R¹¹, and
 - (j) -NO₂,
- (5) heterocycle, wherein heterocycle is selected from:
 - benzoimidazolyl, benzimidazolonyl, benzofuranyl, benzofurazanyl,
 - benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl,
 - 25 carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyll,
 - indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl,
 - naphthpyridinyl, oxadiazolyl, oxazolyl, oxazoline, isoxazoline, oxetanyl, pyranly,
 - pyrazinyl, pyrazolyl, pyridazinyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl,
 - pyrrolyl, quinazolinyll, quinolyl, quinoxalinyll, tetrahydropyranyl, tetrazolyl,
 - 30 tetrazolopyridyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyll, 1,4-dioxanyl,
 - hexahydroazepinyll, piperazinyl, piperidinyll, pyridin-2-onyl, pyrrolidinyl,
 - morpholinyl, thiomorpholinyl, dihydrobenzoimidazolyl, dihydrobenzofuranyl,
 - dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl,
 - dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl,

5 dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl, and N-oxides thereof, which is unsubstituted or substituted with one or more substituents independently selected from:

- (a) -C₁₋₆alkyl,
- (b) -O-C₁₋₆alkyl,
- (c) halo,
- 10 (d) hydroxy,
- (e) phenyl,
- (f) trifluoromethyl,
- (g) -OCF₃;
- (h) -CO₂R⁹,
- 15 (i) -NR¹⁰R¹¹, and
- (j) -CONR¹⁰R¹¹;

R³ is independently selected from the group consisting of:

- (1) hydrogen, and
- 20 (2) -C₁₋₆alkyl;

R⁴ is selected from the group consisting of:

- (1) C₁₋₆alkyl, which is unsubstituted or substituted with halogen, hydroxyl, phenyl or heterocycle,
- 25 (2) C₃₋₇cycloalkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl, and
- (3) phenyl, which is unsubstituted or substituted with one or more substituents independently selected from:
 - (a) -C₁₋₆alkyl,
 - 30 (b) -O-C₁₋₆alkyl,
 - (c) halo,
 - (d) hydroxy,
 - (e) trifluoromethyl,
 - (f) -OCF₃,

- (g) $-\text{CO}_2\text{R}^9$,
(h) $-\text{CN}$,
(i) $-\text{NR}^{10}\text{R}^{11}$,
(j) $-\text{CONR}^{10}\text{R}^{11}$, and
(k) $-\text{NO}_2$;

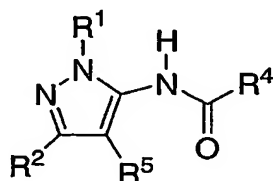
(4) heterocycle, wherein heterocycle is selected from:

benzoimidazolyl, benzimidazolonyl, benzofuranyl, benzofurazanyl,
benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl,
carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolaziny,
indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl,
naphthpyridinyl, oxadiazolyl, oxazolyl, oxazoline, isoxazoline, oxetanyl, pyranyl,
pyrazinyl, pyrazolyl, pyridazinyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl,
pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, tetrahydropyranyl, tetrazolyl,
tetrazolopyridyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidiny, 1,4-dioxanyl,
hexahydroazepinyl, piperazinyl, piperidinyl, pyridin-2-onyl, pyrrolidinyl,
morpholinyl, thiomorpholinyl, dihydrobenzoimidazolyl, dihydrobenzofuranyl,
dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl,
dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl,
dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl,
dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl,
dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl,
dihydrotriazolyl, dihydroazetidiny, methylenedioxybenzoyl, tetrahydrofuranyl,
and tetrahydrothienyl, and N-oxides thereof, which is unsubstituted or substituted
with one or more substituents independently selected from:

- (a) $-\text{C}_{1-6}\text{alkyl}$,
(b) $-\text{O}-\text{C}_{1-6}\text{alkyl}$,
(c) halo,
(d) hydroxy,
(e) phenyl,
(f) trifluoromethyl,
(g) $-\text{OCF}_3$,
(h) $-\text{CO}_2\text{R}^9$,
(i) $-\text{NR}^{10}\text{R}^{11}$, and
(j) $-\text{CONR}^{10}\text{R}^{11}$;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

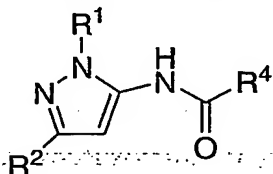
2. The compound of Claim 1 of the formula Ia:



Ia

and pharmaceutically acceptable salts thereof and individual enantiomers and diastereomers thereof.

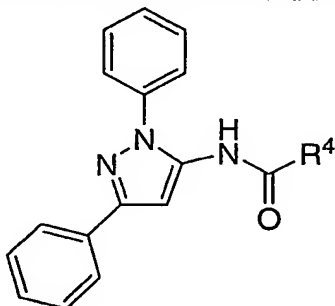
3. The compound of Claim 1 of the formula Ib:



Ib

and pharmaceutically acceptable salts thereof and individual enantiomers and diastereomers thereof.

4. The compound of Claim 1 of the formula Ic:



Ic

and pharmaceutically acceptable salts thereof and individual enantiomers and diastereomers thereof.

5. The compound of Claim 1 wherein R¹ is hydrogen.

6. The compound of Claim 1 wherein R¹ is phenyl.

7. The compound of Claim 1 wherein R² is phenyl.

8. The compound of Claim 1 wherein R³ is hydrogen.

9. The compound of Claim 1 wherein R⁴ is phenyl, which is unsubstituted or substituted with one or more substituents independently selected from:

- (a) -C₁₋₆alkyl,
- (b) -O-C₁₋₆alkyl,
- (c) halo,
- (d) hydroxy,
- (e) trifluoromethyl,
- (f) -OCF₃;
- (g) -CO₂-C₁₋₆alkyl,
- (h) -CN,
- (i) -NH₂,
- (j) -NH-C₁₋₆alkyl,
- (k) -CONH₂, and
- (l) -CONH-C₁₋₆alkyl.

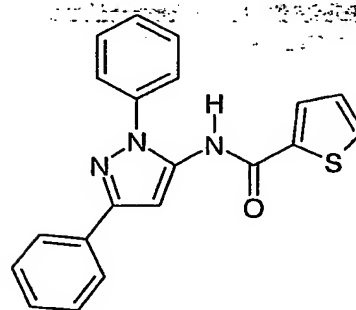
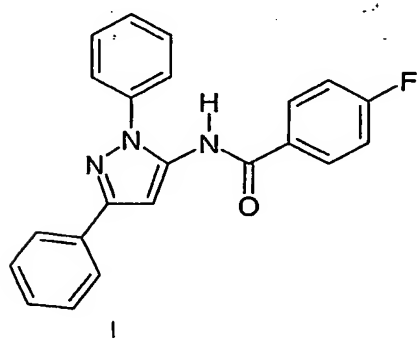
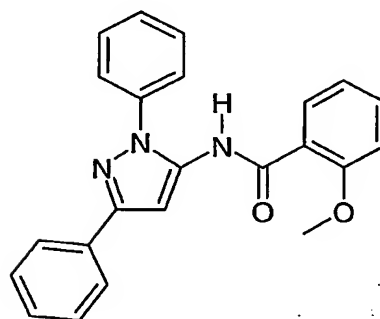
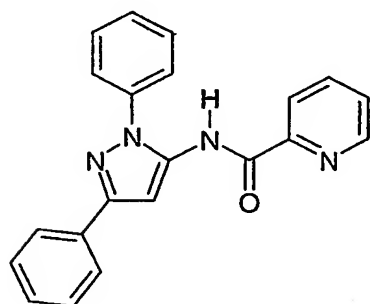
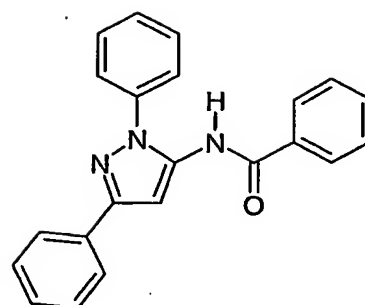
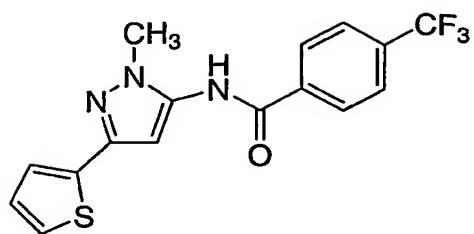
10. The compound of Claim 9 wherein R⁴ is phenyl, which is unsubstituted or substituted with halo or -CN.

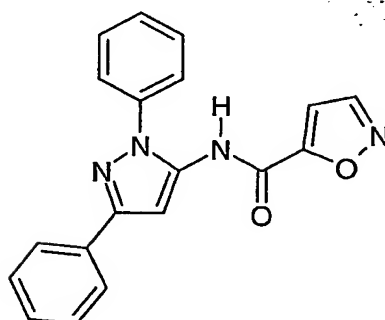
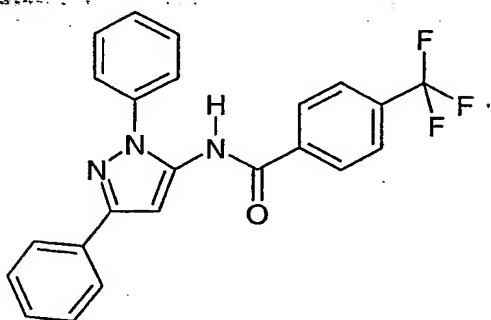
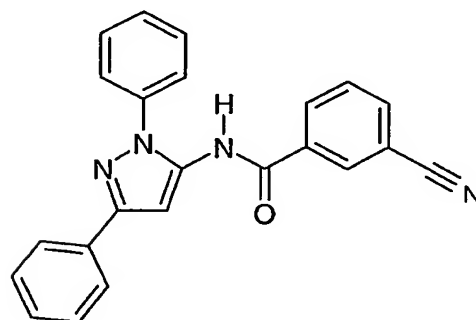
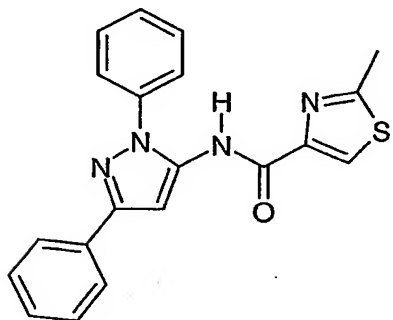
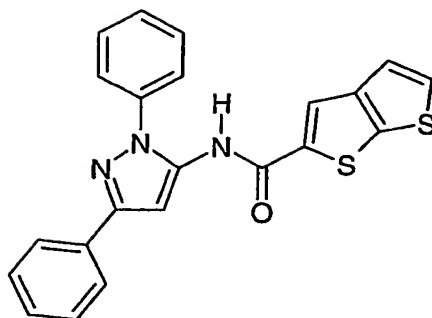
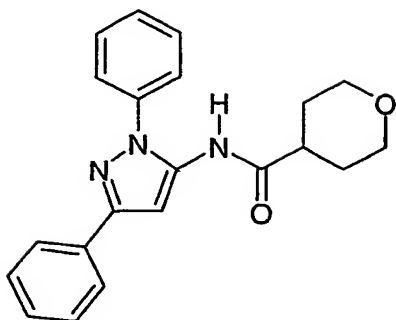
11. The compound of Claim 10 wherein R⁴ is phenyl.

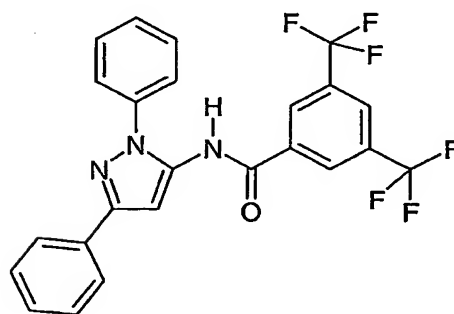
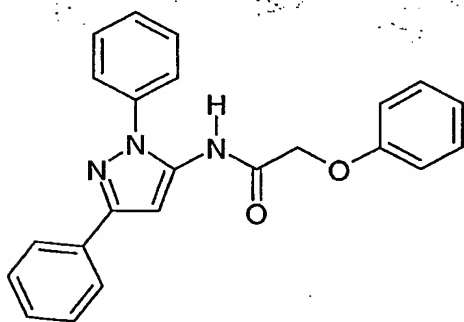
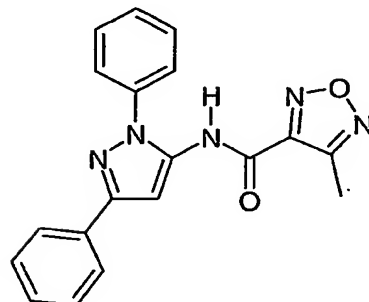
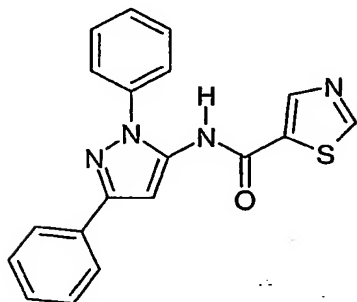
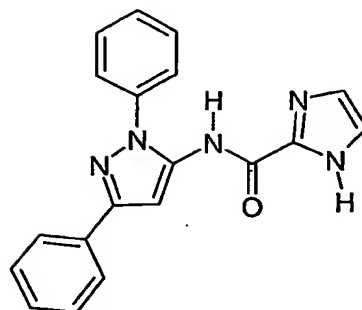
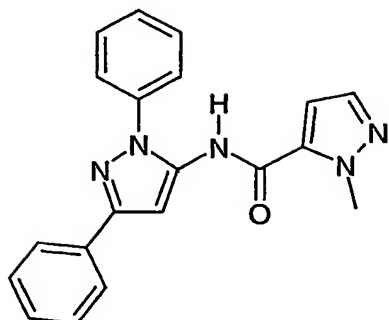
12. The compound of Claim 1 wherein R⁴ is pyridyl.

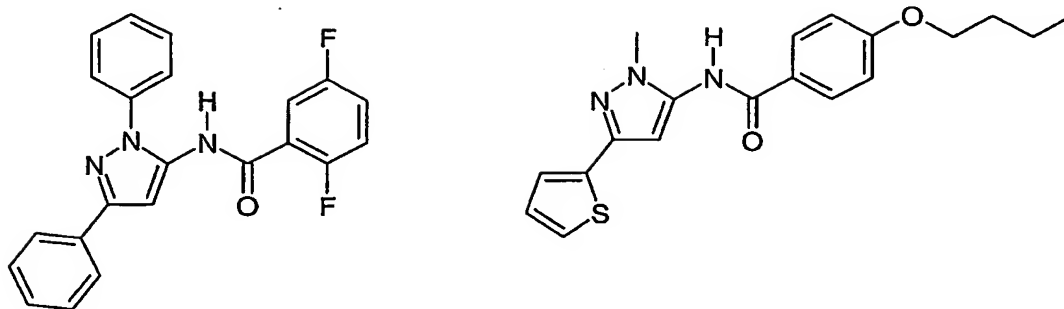
13. The compound of Claim 1 wherein R⁵ is hydrogen.

14. A compound which is selected from the group consisting of:









and pharmaceutically acceptable salts thereof.

15. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

16. A method for potentiation or inhibition of metabotropic glutamate receptor activity in a mammal which comprises the administration of an effective amount of the compound of Claim 1.

17. A method for the manufacture of a medicament for potentiation or inhibition of metabotropic glutamate receptor activity in a mammal comprising combining the compound of Claim 1 with a pharmaceutical carrier or diluent.

18. A method for treating a neurological and psychiatric disorders associated with glutamate dysfunction in a mammalian patient in need of such which comprises administering to the patient a therapeutically effective amount of a compound of Claim 1.

19. A method for treating schizophrenia in a mammalian patient in need of such which comprises administering to the patient a therapeutically effective amount of a compound of Claim 1.

20. A method for treating anxiety in a mammalian patient in need of such which comprises administering to the patient a therapeutically effective amount of a compound of Claim 1.

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☒ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.